JACC Vol. 5, No. 5
May 1985:1161–7

PEDIATRIC CARDIOLOGY

Left Ventricular Wall Stress and Function in Childhood Coarctation of the Aorta

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Unlike most adults with compensated pressure overload of the left ventricle, children with moderate to severe aortic stenosis exhibit pronounced left ventricular muscle hypertrophy, enhanced ejection performance and diminished wall stress. To determine whether these findings are present in other forms of left ventricular pressure overload in children, left ventricular mechanics were studied by catheterization in 14 children with coarctation of the aorta (average peak gradient 39 ± 17 mm Hg) and in 10 normal children. Ejection fraction and mean velocity of circumferential fiber shortening in the coarctation group (0.74 ± 0.09 and 1.71 ± 0.43 circumferences/s, respectively) were significantly higher than in normal subjects (0.65 ± 0.05 and 1.27 ± 0.26 circumferences/s, respectively) ($p = 0.008$), but the ranges for both groups overlapped. End-systolic stress in children with coarctation (77 ± 20 dynes · 10^3/cm^2) was less than in normal children (121 ± 24 dynes · 10^3/cm^2) ($p < 0.001$), again with overlap of the ranges for both groups.

The ratio of end-systolic stress to end-systolic volume index, an estimate of contractile function, was similar in both groups. Relations between severity of obstruction (left ventricular peak systolic pressure, coarctation gradient) and end-systolic stress and between stress and ejection performance were present within the coarctation group. Comparison of these data with those found in children with moderate to severe aortic stenosis shows a similar but less pronounced response to pressure overload due to coarctation of the aorta.

(J Am Coll Cardiol 1985;5:1161–7)

Compensated left ventricular outflow obstruction in adults is associated with muscle hypertrophy, which occurs to offset the increased pressure overload, maintain normal wall stress and preserve normal ejection performance (1,2). In contrast, children with significant left ventricular outflow obstruction due to congenital aortic stenosis or coarctation of the aorta have increased ejection performance (3–5). In children with moderate to severe aortic stenosis, this increased ejection performance results from pronounced muscle hypertrophy and diminished wall stress at rest, which reduce afterload and enhance ejection (5). To determine whether these observations extend to other forms of childhood pressure overload, such as coarctation of the aorta, we studied loading conditions, ejection performance, wall stress and contractile function by cardiac catheterization in a group of children with coarctation of the aorta.

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Methods

Study patients. Fourteen children with coarctation of the aorta underwent right and left heart catheterization. All were asymptomatic with no clinical evidence of heart failure. Although five subjects had abnormalities of the aortic valve identified by echocardiography or angiography, or both, none had associated defects such as aortic stenosis, ventricular septal defect or patent ductus arteriosus. No patient had had previous cardiac surgery.

Ten children made up a normal control group. All underwent catheterization to exclude significant structural heart disease or serious arrhythmia indicated by physical examination and noninvasive studies. No anatomic or hemodynamic abnormalities were found; a normal rhythm was present in all patients during the study.

Written parental consent was obtained before catheterization in all patients. Additional permission was obtained when the investigation required angiography beyond that necessary for routine diagnosis. Total investigational radiation exposure averaged 1,150 mrad per patient.

Catheterization procedure. Catheterization was performed under light sedation with a mixture of meperidine, promethazine and chlorpromazine. The aorta and left heart

0735-1097/85/$3.30

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chambers were entered utilizing the femoral artery approach. Left ventricular and ascending and descending aortic pressures were obtained with a micromanometer-tipped catheter, and peak to peak systolic coarctation gradients were measured using the pullback technique. Pressure recordings were made at 100 mm/s.

Left ventricular mechanics were assessed by single plane anteroposterior angiography with simultaneous micromanometer-tipped catheter recordings from the left ventricle. Contrast medium was injected into the pulmonary artery and the levophase was recorded on the cine film at 60 frames/s (4). To match corresponding pressure waveforms and cine frames, a Q wave marker was placed on the cine film and the onset of the contrast injection was identified on the pressure tracing. Extrasystoles were not encountered using this technique.

Measurements and calculations. Cardiac output was estimated by the Fick method from measurements obtained at the beginning of the catheterization. The levophase of the pulmonary artery angiogram was examined, and two to five cardiac cycles were selected for optimal chamber opacification and endocardial definition; when possible, cycles at end-expiration were chosen. After the corresponding left ventricular pressure recordings were identified, calculations were performed for each cycle and averaged to obtain data for each patient.

Left ventricular volumes were calculated by the area-length method and the appropriate regression equation (6). End-diastole was defined at the Q wave marker and end-systole as the smallest volume measured; in nearly all cases, the latter corresponded with aortic valve closure. All volumes were indexed to body surface area and the ejection fraction calculated. The mean velocity of circumferential fiber shortening (Vcf) was calculated from the expression $Vcf = (EDD - ESD)/(EDD \cdot ET)$, where EDD and ESD are the end-diastolic and end-systolic minor dimensions, respectively, and ET is the ejection time measured between aortic valve opening and closure. Wall thickness was measured at the mid portion of the left ventricular cavity at end-diastole and left ventricular mass was estimated by the method of Kennedy et al. (6).

The end-systolic pressure was obtained from the left ventricular pressure recording at the time corresponding to end-systole, previously determined by angiography. End-systolic circumferential wall stress was estimated utilizing the approximation of Hugenholtz et al. (7) for wall thickness during systole and the formula of Mirsky (8). The ratio of end-systolic stress to end-systolic volume index, an estimate of contractile function, was calculated.

Validation of measurements and statistical methods. We have previously described (5) small inter- and intraobserver variations in volume determinations and validation of the small end-systolic volumes encountered in the pressure overload group. All values are expressed as an average ± 1 standard deviation. Comparisons between the averages of measured and calculated variables in both patient groups were made using an unpaired *t* test. Regression was performed by the method of least squares.

Results

Pressure, volume and calculated variables for individual patients in the control and coarctation groups are given in Tables 1 and 2, respectively. The average age was 7.9 ± 3.3 years in the control group and 6.6 ± 4.6 years in the coarctation group (NS). The average body surface area in the control group was 1.05 ± 0.28 m^2 and 0.95 ± 0.47 m^2 in the coarctation group (NS).

Hemodynamic variables. The average heart rate in the coarctation group (114 ± 27 beats/min) was higher than in

Table 1. Pressure, Volume and Derived Data for 10 Control Subjects

Case	Age (yr)	BSA (m^2)	HR (beats/min)	LVPSP (mm Hg)	LVEDP (mm Hg)	LVESP (mm Hg)	LVEDVI (cc/m^2)	LVESVI (cc/m^2)	CI (liters/min per m^2)	EF	Vcf (circ/s)	LVMI (g/m^2)	LVESS (d·10^3/cm^2)	LVESS / LVESVI
1	8	1.27	83	110	7	70	89	27	5.2	0.70	1.57	111	108	4.0
2	7	1.20	71	110	5	51	58	22	2.6	0.61	0.99	81	130	5.8
3	11	1.23	79	108	6	72	88	24	5.0	0.72	1.53	115	98	4.0
4	10	1.20	78	95	5	55	69	22	3.7	0.68	0.82	99	96	4.3
5	3	0.66	112	90	5	75	64	23	4.6	0.64	1.20	130	156	6.9
6	3	0.66	112	95	9	80	75	30	5.1	0.60	1.25	144	163	5.4
7	11	1.10	74	102	5	65	90	35	4.1	0.62	1.18	118	105	3.0
8	5	0.79	98	110	6	73	59	18	4.1	0.70	1.67	117	101	5.7
9	9	0.93	77	98	4	80	84	29	4.2	0.65	1.31	130	120	4.1
10	12	1.50	73	114	8	85	66	27	2.8	0.58	1.14	100	135	4.9

BSA = body surface area; circ/s = circumferences/s; CI = cardiac index; d = dynes; EF = ejection fraction; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVEDVI = left ventricular end-diastolic volume index; LVESP = left ventricular end-systolic pressure; LVESS = left ventricular end-systolic stress; LVESVI = left ventricular end-systolic volume index; LVMI = left ventricular mass index; LVPSP = left ventricular peak systolic pressure; Vcf = velocity of circumferential fiber shortening.

Table 2. Pressure, Volume and Derived Data for 14 Patients With Coarctation of the Aorta

Case	Age (yr)	BSA (m^2)	HR (beats/min)	LVPSP (mm Hg)	LVEDP (mm Hg)	Grad (mm Hg)	LVESP (mm Hg)	LVEDVI (cc/m^2)	LVESVI (cc/m^2)	CI (liters/min per m^2)	EF	Vcf (circ/s)	LVMI (g/m^2)	LVESS ($d \cdot 10^3/cm^2$)	LVESS / LVESVI
11	16	2.03	75	107	13	20	92	87	30	4.3	0.66	1.17	129	108	3.6
12	7	0.82	150	105	7	30	75	57	18	5.8	0.68	1.80	125	75	4.1
13	9	0.92	150	150	6	50	70	62	21	6.1	0.67	1.80	139	56	2.7
14	2	0.46	112	105	10	50	70	87	35	5.9	0.60	1.40	207	91	2.6
15	11	1.42	84	95	10	25	75	94	25	5.8	0.74	1.56	120	100	4.1
16	4	0.76	112	120	13	40	60	50	12	4.3	0.76	1.57	131	67	5.7
17	9	1.02	95	135	10	63	110	63	7	5.3	0.89	2.20	125	71	10.0
18	1	0.50	120	100	5	30	70	36	10	3.1	0.72	1.10	163	99	10.0
19	3	0.76	109	160	12	55	90	49	13	3.9	0.73	1.63	131	71	5.4
20	3	0.60	116	130	4	40	115	53	17	4.2	0.69	1.68	180	69	4.1
21	14	1.74	67	130	10	20	65	57	21	2.4	0.63	1.21	92	98	4.6
22	3	0.64	150	150	10	65	90	66	8	8.7	0.88	2.08	224	41	5.2
23	7	1.01	116	112	10	10	95	69	13	6.5	0.81	2.20	109	75	5.8
24	4	0.68	138	120	10	52	110	34	4	4.1	0.87	2.57	138	58	13.0

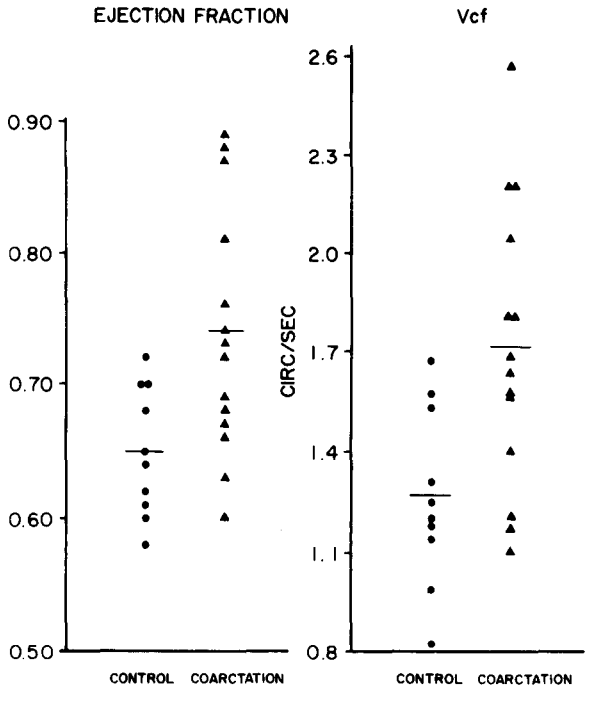
Grad = peak to peak systolic coarctation gradient; other abbreviations as in Table 1.

the control group (86 ± 16 beats/min) ($p = 0.008$), but there was no significant difference between cardiac index in the control and coarctation groups (4.1 ± 0.9 and 5.0 ± 1.6 liters/min per m^2, respectively).

Left ventricular volumes and pump function. The average left ventricular end-diastolic volume index in the coarctation group (62 ± 18 cc/m^2) was slightly less than in the control group (74 ± 13 cc/m^2), but the difference was not significant. Average left ventricular end-systolic volume index was reduced in the coarctation group (16.7 ± 0.9 cc/m^2) in comparison with the control group (26.0 ± 5.0 cc/m^2) ($p < 0.002$). The average ejection fraction and average mean velocity of circumferential fiber shortening in the coarctation group (0.74 ± 0.09 and 1.71 ± 0.43 circumferences/s, respectively) were greater than in the control group (0.65 ± 0.05 and 1.27 ± 0.26 circumferences/s, respectively) ($p = 0.008$), but for both variables there was substantial overlap between the two study groups (Fig. 1). Within each of the study groups, there was no significant relation between heart rate and end-diastolic volume index, end-systolic volume index, ejection fraction or mean velocity of circumferential fiber shortening.

Ventricular mechanics. Moderate left ventricular hypertrophy was present in the children with coarctation; the average left ventricular mass index was greater in this group (144 ± 37 g/m^2) than in the control group (115 ± 18 g/m^2) ($p = 0.03$). The average left ventricular peak systolic and end-diastolic pressures were higher in the coarctation group (123 ± 20 and 9.0 ± 3.0 mm Hg) than in the control group (103 ± 8 and 6.0 ± 1.6 mm Hg) ($p = 0.002$). The average coarctation pressure gradient was 39 ± 17 mm Hg. Despite increased left ventricular peak systolic pressure, the average left ventricular end-systolic wall stress was reduced in the children with coarctation (77 ± 20 dynes · $10^3/cm^2$) in comparison with the control group (121 ± 24 dynes · $10^3/cm^2$) ($p < 0.001$) (Fig. 2). As with variables of pump function (ejection fraction, mean velocity of circumferential fiber shortening), there was some overlap between the two study groups. The ratio of left ventricular end-systolic wall stress to end-systolic volume index in all but three patients with coarctation coincided with that of control subjects (Fig. 3); the average value in the coarctation group (5.5 ± 3.1) was

Figure 1. Ejection fraction and mean velocity of circumferential fiber shortening (Vcf) for control subjects (**circles**) and patients with coarctation of the aorta (**triangles**). The average value (**horizontal line**) for each variable is significantly greater in the coarctation group ($p = 0.008$), but there is considerable overlap between study groups. CIRC/SEC = circumferences per second.



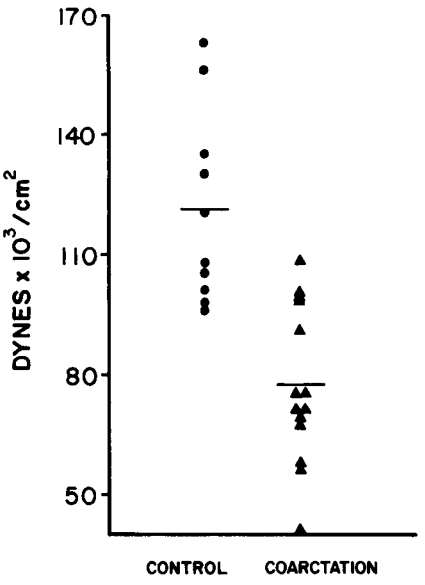
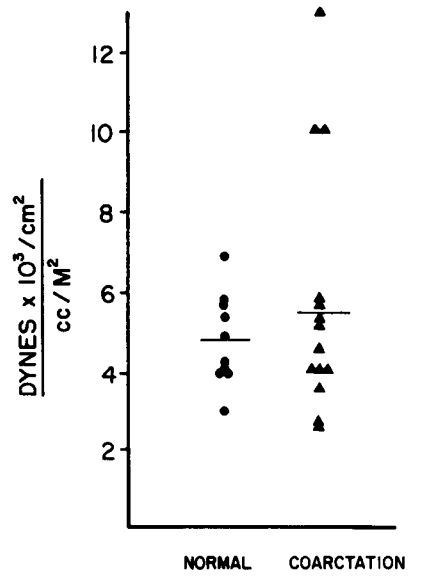


Figure 2. End-systolic stress for control subjects (**circles**) and patients with coarctation of the aorta (**triangles**). The average value (**horizontal line**) is significantly lower in the coarctation group ($p < 0.001$).

similar to that of the control group (4.8 ± 1.1). There was no relation between heart rate and the ratio of end-systolic stress to end-systolic volume index within either group.

An inverse relation between end-systolic stress and muscle shortening was present in children with coarctation. Figure 4 demonstrates the correlation between left ventricular end-systolic wall stress and the mean velocity of circumferential fiber shortening. There was also an inverse relation between the severity of obstruction (left ventricular peak systolic pressure, coarctation gradient) and end-systolic wall stress (Fig. 5). There was no relation between severity of obstruction and either mean velocity of circumferential fiber shortening or ejection fraction.

Figure 3. The ratio of end-systolic wall stress to end-systolic volume index. This ratio, an estimate of contractile function, was similar in the control (**circles**) and coarctation (**triangles**) groups. The **horizontal line** represents the average value for each group.



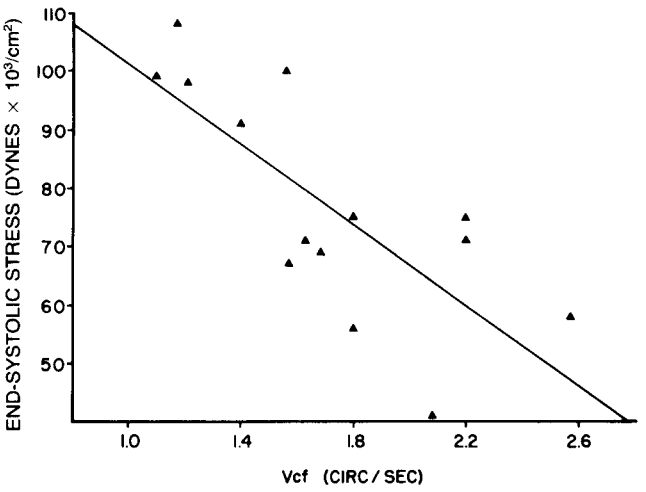


Figure 4. Relation between afterload and ejection performance in patients with coarctation of the aorta. This is demonstrated by the inverse relation between end-systolic stress and mean velocity of circumferential fiber shortening (Vcf) ($p = 0.01$, $r = 0.71$).

Discussion

Ventricular hypertrophy, wall stress and pump function. This study of children with coarctation of the aorta demonstrates reduced end-systolic wall stress and enhanced pump function despite increased left ventricular peak systolic pressure. These data are parallel with the findings in children with congenital aortic stenosis (5), but the magnitude of the phenomenon appears less marked. Hypertrophy in adults with compensated left ventricular outflow obstruction usually occurs to maintain normal wall stress and pump function (1,2). However, the amount of hypertrophy may vary, altering wall stress and pump function independent of contractile state (9–11). Whether hypertrophy is adequate or inadequate, an inverse relation exists between stress and muscle shortening (9–12). Unlike adults with pressure overload, our children with coarctation exhibit pronounced hypertrophy, reduced wall stress at rest and enhanced shortening at rest. However, like adults, children with pressure overload exhibit an inverse relation between afterload and ejection performance (Fig. 4). Therefore, it seems likely that subnormal afterload is responsible for the enhanced ejection performance.

Assessment of pressure overload and muscle hypertrophy. The increased average left ventricular peak systolic pressure in our patients with coarctation is slightly less than but compares favorably with that found by Graham et al. (4) in a nearly identical group of children. The average left

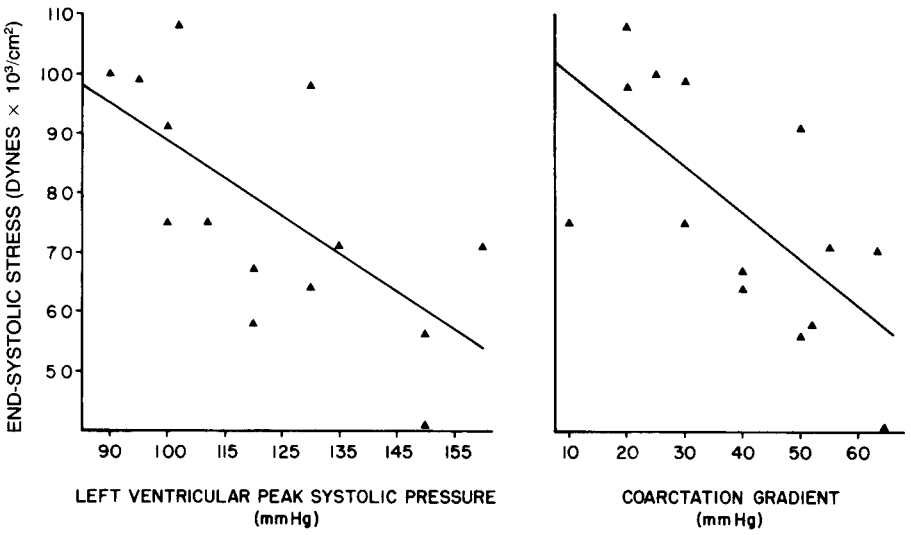


Figure 5. Relation between severity of obstruction and wall stress in patients with coarctation. This is shown by the inverse relation of left ventricular peak systolic pressure (**left**) and coarctation gradient (**right**) to end-systolic wall stress ($p = 0.01$, $r = 0.68$).

ventricular mass index is also similar (4). The small but significant increase in average left ventricular end-systolic pressure in the coarctation group was parallel with the increase in average peak systolic pressure.

Interpretation of left ventricular volumes and pump function. The average left ventricular end-diastolic volume index in both the control and coarctation groups is similar to that obtained by Graham et al. (4). Although the average end-diastolic volume index in the coarctation group was slightly less than that in the control group, the significant reduction of the average end-systolic volume index in the same group was associated with the enhanced ejection performance we observed. That ejection fraction is increased in the coarctation group also agrees closely with published data (3,4). Figure 1 shows that although there is separation of the average ejection fraction and average mean velocity of circumferential fiber shortening between the normal and control groups, there is considerable overlap among individual patients of both groups. Therefore, enhanced pump function in coarctation of the aorta is not always present. In addition, the severity of obstruction found in individual children within the coarctation group may not serve as a guide to expected pump function because we found no significant relation between left ventricular peak systolic pressure or coarctation gradient and either ejection fraction or mean velocity of circumferential fiber shortening. The lack of correlation is surprising because a relation exists between severity of obstruction and end-systolic wall stress (Fig. 5) and between stress and shortening (Fig. 4). The modest degree of correlation in these two relations and wide variation of end-diastolic volume index among patients with coarctation are probably responsible for the lack of a significant correlation between severity of obstruction and enhancement of pump function.

Interpretation of end-systolic stress data. The reduction of end-systolic stress that occurs in the presence of increased left ventricular end-systolic pressure in patients with coarctation is presumably due to pronounced muscle hypertrophy and wall thickening. However, end-systolic stress in four of the patients with coarctation fell within the range of that in our control subjects. The coarctation gradients in all four of the children (Cases 11,15,18 and 21) were well below the average and among the mildest of the group. Conversely, patients with coarctation with a gradient significantly greater than the group average tended to have lower end-systolic stress (Fig. 5), suggesting that the severity of obstruction influences the degree to which pronounced muscle hypertrophy occurs. Muscle hypertrophy, reflected in the left ventricular mass index, was inversely related to end-systolic stress in those patients with coarctation with a gradient greater than the group mean ($r = -0.64$, $p = 0.04$), but there was no relation between left ventricular mass index and end-systolic stress for the coarctation group as a whole. This further supports the observations that pronounced hypertrophy and diminished wall stress are associated with greater degrees of obstruction and that children with a milder coarctation gradient exhibit "appropriate" hypertrophy which maintains a normal wall stress.

Measurement of left ventricular contractile function. Many reports (9,13–15) suggest that contractile function in adults with pressure overload may be normal or reduced and varies with the severity and duration of the disease. In contrast, contractile function in children with chronic left ventricular obstruction has not been studied extensively. Using isovolumic indexes, Graham et al. (16) calculated maximal velocity of shortening (V_{max}) indexes in a group of asymptomatic children with various degrees of obstruction due to aortic stenosis and coarctation of the aorta. In most patients, V_{max} was within the normal range when developed pressure was used, but was reduced when derived from total pressure. However, because end-diastolic pressure was increased in the group with obstruction, and

because the total pressure method is more sensitive to loading conditions, it is likely that the developed pressure method was more reflective of muscle function (9,17). Therefore, muscle function may have been normal in the patients studied by Graham et al.

In the present study, contractile function was estimated by the ratio of end-systolic stress to end-systolic volume index. The linear relation between stress and volume at end-systole, derived from multiple afterload manipulations, is independent of loading conditions and has been used for the evaluation of contractile function (18–23). Although we recognize the differences between our method and the true end-systolic relation (24), we found the ratio to be clinically useful (25–29). For most patients with coarctation of the aorta, the ratio of end-systolic stress to end-systolic volume index was in the range of our control subjects. Three children had a ratio considerably greater than the control range; this is probably due to the significant effect of minor variations in our small end-systolic volumes on the value of the ratio. Consideration of the data obtained by Graham et al. (16), data collected in children with severe aortic stenosis (5) and our data suggests that contractile function is normal in asymptomatic children with widely different degrees of pressure overload.

Effect of heart rate on ventricular volumes, pump function and contractile function. The higher average heart rate in the coarctation group and the wide distribution of heart rates in both groups of children may be related, in part, to the slightly lower average age of the patients with coarctation and the wide distribution of ages in both groups. Examination of outpatient echocardiograms performed in most of the patients with coarctation and the control subjects showed an average heart rate in the patients with coarctation that was slightly higher but not significantly different from that of control subjects. This is consistent with the small difference in average age between the two groups and suggests that there is no intrinsic "hyperadrenergic" state associated with coarctation of the aorta. No such state was present in the study of children with aortic stenosis (5). It is unlikely that increased heart rate or a transient "hyperadrenergic" state during catheterization was responsible for our results because there was no relation between heart rate and left ventricular volume indexes, ejection fraction, mean velocity of circumferential fiber shortening or the ratio of end-systolic wall stress to end-systolic volume index within either group.

Comparison with results in children with aortic stenosis. In comparison with similar data obtained in children with moderate to severe aortic stenosis (5), our children with coarctation of the aorta exhibited enhanced pump function and diminished wall stress of a milder degree. Ranges for ejection fraction and mean circumferential fiber shortening in the aortic stenosis and control groups were nearly exclusive. The average end-systolic stress in the patients with aortic stenosis was less than one-fourth that of the control group and the ranges for end-systolic stress in both groups were widely separated. This contrasts with the overlap of pump function and stress data in our patients with coarctation and control subjects (Fig. 1 and 2). The average left ventricular peak systolic pressure and average systolic gradient in the aortic stenosis group were substantially higher than those in our patients with coarctation. Although there was no significant correlation between severity of obstruction and pump function within either the coarctation or the aortic stenosis group (5), these group comparisons suggest that severity of obstruction may influence the magnitude of pronounced hypertrophy, diminished wall stress and enhanced pump function.

Conclusions. The phenomenon of pronounced hypertrophy, enhanced pump function and diminished wall stress at rest in asymptomatic children with moderate to severe aortic stenosis has been extended to children with coarctation of the aorta. These findings suggest a general response to pressure overload in children that differs in some ways from the response of adults. The magnitude of these changes is considerably less in patients with coarctation, perhaps related to the milder degree of obstruction normally found in coarctation of the aorta. Therefore, practical application of this phenomenon may be severely limited (30). The mechanisms governing muscle hypertrophy in children with left ventricular pressure overload have not been explained completely and require further investigation.

We express our appreciation to Marianna Donleavy for her help in preparing the manuscript.

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